

Appln No.: 10/019,200
Amendment Dated: February 9, 2006
Reply to Office Action of November 10, 2005

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-24. (canceled)

25. (withdrawn) An apparatus for preparation of a lipid vesicles comprising:
(a) a first reservoir for receiving a buffer composition;
(b) a static mixer for agitating buffer composition in the first reservoir;
(c) a second reservoir for receiving a lipid solution;
(d) a dispensing head for introducing lipid solution from the second reservoir into the first reservoir, and
(e) a connector joining the second reservoir to the dispensing head for conducting lipid solution from the second reservoir to the dispensing head, wherein the dispensing head has formed therein one or more injection ports having a diameter of 2 mm or less.

26. (withdrawn) The apparatus of claim 25, wherein the first reservoir contains a citrate buffer and the second reservoir contains an ethanolic lipid solution comprising from about 1 to about 100 mg/ml lipid in at least 90% by weight ethanol.

27. (withdrawn) The apparatus of claim 26, wherein the dispensing head has a plurality of injection ports formed therein.

28. (withdrawn) The apparatus of claim 27, wherein the dispensing head has twenty or more injection ports formed therein.

29. (withdrawn) The apparatus of claim 25, wherein the dispensing head has a plurality of injection ports formed therein.

30. (withdrawn) The apparatus of claim 25 wherein the dispensing head has twenty or more injection ports formed therein.

31. (currently amended) A method of making lipid vesicles comprising:
(a) preparing a solution of ethanolic lipid comprising from about 1 to about 100 mg/ml lipid in at least 90% by weight ethanol per weight of solvent;
(b) injecting the ethanolic lipid directly into aqueous buffer through an injection port of diameter about 2 mm or less to make a lipid/buffer mixture; and

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(c) mixing the lipid/buffer mixture by turbulent passage through a static mixer to produce lipid vesicles, wherein the resulting lipid vesicles, prior to any extrusion step, are in about 10% or more by weight ethanol per weight of the lipid/buffer mixture, and have average diameter of from about 80 nm to about 200 nm.

32. (original) The method of claim 31, wherein the buffer has pH below 5.0

33. (original) The method of claim 31, wherein the buffer has a concentration of divalent cation greater than about 100 mM.

34. (original) The method of claim 31, wherein the ethanolic lipid comprises sphingomyelin

35. (original) The method of claims 31, wherein the ethanolic lipid comprises cholesterol

36. (original) The method of claims 31, wherein the ethanolic lipid comprises sphingomyelin and cholesterol in a ratio by weight of from about 1:4 to about 4:1.

37. (original) The method of claim 31, wherein the ethanolic lipid comprises a PEG-lipid conjugate, a cationic lipid, and a neutral lipid.

38. (original) The method of claim 37, wherein the lipid in the ethanolic lipid comprises a PEG-lipid conjugate, a cationic lipid, a neutral lipid, and cholesterol in a ratio by weight of about 5: 25:25:45.

39. (original) The method of claim 31, wherein the concentration of lipid in the ethanolic lipid is less than about 50mM.

40. (original) The method of claim 31, wherein the concentration of lipid in the ethanolic lipid is less than about 25 mg/ml.

41. (currently amended) The method of claim 31, wherein said turbulence turbulent passage, measured by Nre, is greater than about 2000.

42. (currently amended) The method of claim 41, wherein said turbulence turbulent passage, measured by Nre, is greater than 3000.

43. (original) The method of claim 31, wherein said average diameter is from about 100 nm to about 130 nm.

44. (withdrawn) An apparatus for making empty unilamellar liposomes comprising:

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(a) a first feeder tank containing an ethanolic lipid;
(b) a second feeder tank containing an aqueous buffer;
(c) a combining chamber disposed to receive and combine outflow of the first feeder tank with outflow of the second feeder tank, said combining chamber comprising an injection port of diameter 2mm or less; and

(d) a static mixer means for mixing the product of the combining chamber to form unilamellar lipid vesicles in 5 - 50% ethanol, said vesicles, prior to any extrusion, having average diameter of from about 80 nm to about 200 nm.

45. (withdrawn) The apparatus of claim 44, further comprising

- e) a reservoir for receiving the product of the static mixer means; and
- f) a continuous flow extrusion circuit operably connected to the reservoir.

46. (withdrawn) The apparatus of claim 44, further comprising

- e) a reservoir for receiving the product of the static mixer means; and
- f) a dialysis or diafiltration system operably connected to the reservoir.

47. (withdrawn) The apparatus of claim 44, wherein the Nre of the static mixer means is > 2000.

48. (withdrawn) The apparatus of claim 44, with the proviso that no continuous flow solvent removal means is incorporated with elements c) through e).

49. (withdrawn) The apparatus of claim 44, wherein the combining chamber combines the outflow of the first feeder tank with outflow of the second feeder tank in a volumetric ratio of from about 1:20 to about 2:1.